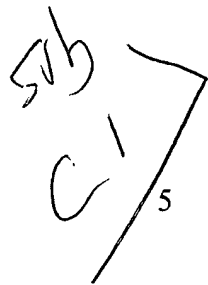


We claim:



1. An antibacterial agent, which comprises a non-pathogenic donor bacterial cell harboring at least one transmissible plasmid comprising:
a) an origin of replication for synthesizing the plasmid in a bacterial cell, wherein initiation of replication at the origin is negatively controlled by a plasmid replication repressor;

b) an origin of transfer from which conjugative transfer of the transmissible plasmid initiates from the donor cell to at least one recipient cell; and,
10 optionally,

c) at least one screenable marker gene;

wherein the donor cell further comprises one or more transfer genes conferring upon the donor cell the ability to conjugatively transfer the transmissible plasmid to the recipient cell, and wherein the donor cell produces the plasmid replication repressor, and further wherein the at least one recipient cell is a pathogenic bacterium
15 that does not produce the plasmid replication repressor.

000000000000000000000000

10

15

20

2. The antibacterial agent of claim 1, wherein the transfer genes are contained on a helper plasmid within the donor cell, such that the transmissible plasmid is transmissible from the donor cell to a recipient cell, but is not further self-transmissible from the recipient cell to another recipient cell.

25

3. The antibacterial agent of claim 1, wherein the transfer genes are contained on the transmissible plasmid, such that the transmissible plasmid is self-transmissible from the donor cell to a recipient cell, and further from the recipient cell to another recipient cell.

4. The antibacterial agent of claim 1, wherein the transmissible plasmid comprises a derivative of a naturally-occurring transmissible plasmid containing a gene

encoding the replication repressor that has been mutated to produce a non-functional replication repressor.

5 5. The antibacterial agent of claim 4, wherein the naturally-occurring transmissible plasmid is selected from the group consisting of RK2, R6K, pCU1, p15A, pIP501, pAM β 1 and pCRG1600.

10 6. The antibacterial agent of claim 5, wherein the naturally-occurring plasmid is R6K and the mutation comprises a mutation in the R6K *pir* gene such that its encoded π protein comprises an at least one amino acid deletion or substitution at amino acids 105, 106 or 107.

15 7. The antibacterial agent of claim 1, wherein the donor cell is a non-pathogenic strain of bacteria selected from the group consisting of *Escherichia coli*, *Lactobacillus spp.*, *Lactococcus*, *Bifidobacteria*, *Eubacteria*, and bacterial minicells.

20 8. The antibacterial agent of claim 1, wherein the recipient cell is a pathogenic strain of bacterium selected from the group consisting of *Campylobacter spp.*, *Enterobacter spp.*, *Enterococcus spp.*, *Escherichia coli*, *Gardnerella vaginalis*, *Haemophilus spp.*, *Helicobacter pylorii*, *Mycobacterium tuberculosis*, *Propionobacter acnes*, *Pseudomonas aeruginosa* and other *Pseudomonas spp.*, *Salmonella typhimurium*, *Shigella spp.* and *Staphylococcus spp.*

25 9. The antibacterial agent of claim 1, wherein the origin of replication is derived from a plasmid selected from the group consisting of R6K, RK2, rts1, p15A and RSF1010.

10. The antibacterial agent of claim 1, wherein the origin of replication is selected from the group consisting of F and P1.

03727560

ab
1

11. The antibacterial agent of claim 1, wherein the screenable marker gene confers a nutritional selection advantage on cells containing the transmissible plasmid.

5 12. The antibacterial agent of claim 1, wherein the transfer genes are derived from a plasmid selected from the group consisting of F, R6K and Ti.

10 13. A method of treating a patient for a pathogenic bacterial infection, which comprises administering to the patient the antibacterial agent of claim 1 in a manner such that the donor cells of the antibacterial agent come into conjugative proximity to the pathogenic bacterial cells, such that the transmissible plasmids of the donor cells are transferred from the donor cells to the pathogenic bacterial cells, whereupon the transmissible plasmids commence unchecked replication, thereby killing the pathogenic bacterial cells.

15 14. A pharmaceutical preparation for treating a patient for a bacterial infection, comprising the antibacterial agent of claim 1 formulated for a pre-determined route of administration to the patient.

20 15. The pharmaceutical preparation of claim 14, wherein the pre-determined route of administration is selected from the group consisting of: topical, oral, nasal, pulmonary, ophthalmic, aural, rectal, urogenital, subcutaneous, intraperitoneal and intravenous.

sub
C1
25

16. An antibacterial agent, which comprises a non-pathogenic donor bacterial cell harboring at least one transmissible plasmid comprising:

- a) an origin of replication for synthesizing the plasmid in a bacterial cell;
- b) an origin of transfer from which conjugative transfer of the transmissible plasmid initiates from the donor cell to at least one recipient cell;

c) at least one killer gene that, upon expression in a bacterial cell, produces a product that kills the cell; and, optionally,

d) at least one screenable marker gene;

5 wherein the donor cell further comprises one or more transfer genes conferring upon the donor cell the ability to conjugatively transfer the transmissible plasmid to the recipient cell, and wherein the donor cell is modified so as to be unaffected by the product of the killer gene, and further wherein the at least one recipient cell is a pathogenic bacterium that has not been modified so as to be unaffected by the product of the killer gene.

10

17. The antibacterial agent of claim 16, wherein the transfer genes are contained on a helper plasmid within the donor cell, such that the transmissible plasmid is transmissible from the donor cell to a recipient cell, but is not further self-transmissible from the recipient cell to another recipient cell.

15

18. The antibacterial agent of claim 16, wherein the transfer genes are contained on the transmissible plasmid, such that the transmissible plasmid is self-transmissible from the donor cell to a recipient cell, and further from the recipient cell to another recipient cell.

20

19. The antibacterial agent of claim 16, wherein the killer gene kills the cells by being expressed and thereby producing a gene product that is detrimental or lethal to bacterial cells, and the donor cells have been modified so as to repress the expression of the killer gene, thereby avoiding production of the detrimental or lethal gene product.

25

20. The antibacterial agent of claim 16, wherein the killer gene is obtained from a bacteriophage.

00000000000000000000

slb
ci

21. The antibacterial agent of claim 20, wherein the bacteriophage is selected from the group consisting of T-series phages, P1, p22 and λ .

5 22. The antibacterial agent of claim 16, wherein the donor cell is a non-pathogenic strain of bacteria selected from the group consisting of *Escherichia coli*, *Lactobacillus spp.*, *Lactococcus*, *Bifidobacteria*, *Eubacteria*, and bacterial minicells.

10 23. The antibacterial agent of claim 16, wherein the recipient cell is a pathogenic strain of bacterium selected from the group *Campylobacter spp.*, *Enterobacter spp.*, *Enterococcus spp.*, *Escherichia coli*, *Gardnerella vaginalis*, *Haemophilus spp.*, *Helicobacter pylorii*, *Mycobacterium tuberculosis*, *Propionobacter acnes*, *Pseudomonas aeruginosa* and other *Pseudomonas spp.*, *Salmonella typhimurium*, *Shigella spp.* and *Staphylococcus spp.*

15 24. The antibacterial agent of claim 16, wherein the origin of replication is derived from a plasmid selected from the group consisting of R6K, RK2, rts1, p15A and RSF1010.

20 25. The antibacterial agent of claim 16, wherein the origin of replication is selected from the group consisting of F and P1.

25 26. The antibacterial agent of claim 16, wherein the screenable marker gene confers a nutritional selection advantage on cells containing the transmissible plasmid.

27. The antibacterial agent of claim 16, wherein the transfer genes are derived from a plasmid selected from the group consisting of F, R6K and Ti.

28. A method of treating a patient for a pathogenic bacterial infection,

000000000000000000000000

which comprises administering to the patient the antibacterial agent of claim 16 in a manner such that the donor cells of the antibacterial agent come into conjugative proximity to the pathogenic bacterial cells, such that the transmissible plasmids of the donor cells are transferred from the donor cells to the pathogenic bacterial cells, whereupon the at least one killer gene is expressed, thereby producing the product that kills the pathogenic bacterial cells.

5

29. A pharmaceutical preparation for treating a patient for a bacterial infection, comprising the antibacterial agent of claim 16 formulated for a pre-determined route of administration to the patient.

10

30. The pharmaceutical preparation of claim 29, wherein the pre-determined route of administration is selected from the group consisting of: topical, oral, nasal, pulmonary, ophthalmic, aural, rectal, urogenital, subcutaneous, intraperitoneal and intravenous.

15

4/10/31

030303 06275366